

# Exercise and Physical Activity in Marfan Syndrome and Related Disorders

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**WARNING**

EXERCISE  
HAS BEEN KNOWN  
TO CAUSE HEALTH  
& HAPPINESS



# Benefits of Routine Exercise: Health and Well-Being

## Cardiovascular

- Lower HR, BP
- Lower cholesterol
- Less coronary disease
- Lower risk of heart attack and stroke

## Musculoskeletal

- less osteoporosis
- less back pain
- balance

Lower blood sugar

Longer life



Social aspects

Weight loss

Lower risk of colon and breast cancer

Mental health

- Less depression
- Less anxiety
- Improved mood
- Improved memory

How do we counsel individuals with hereditary aortic disease (Marfan, Loeys-Dietz, FTAA, vEDS) regarding exercise, both for the athlete and non-athlete?

What type of exercise is safe?

How much exercise is safe?

Do we always have the **right** answer?

We typically err on the side of safety...

We do not have any outcomes data in this area to guide us.

# Physical Activity Concerns in Marfan Syndrome and Related Disorders

## Ocular

retinal detachment, lens dislocation

## Musculoskeletal

back, feet, hips

## Pulmonary

pneumothorax, restrictive lung disease

## Cardiovascular

cardiomyopathy

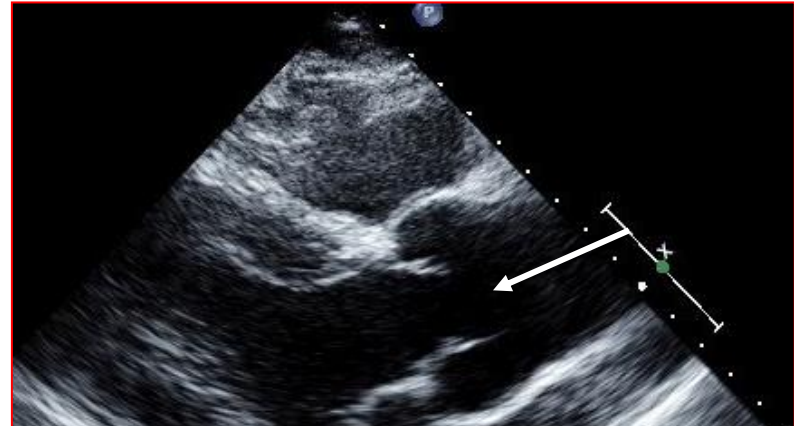
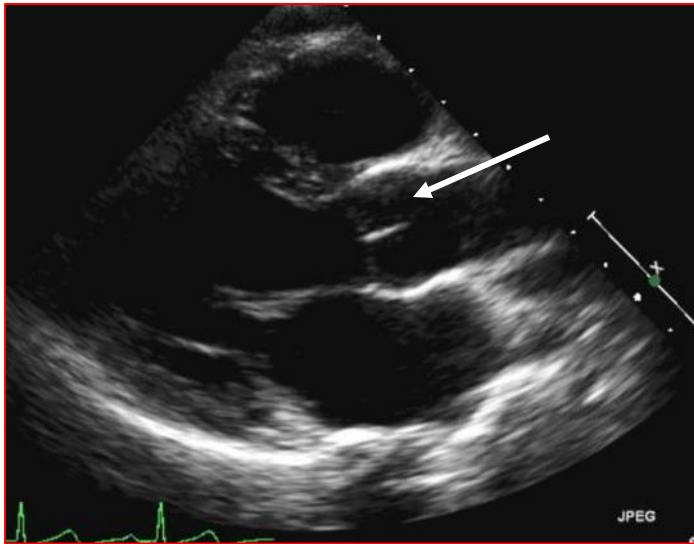
valvular disease

arrhythmias

mechanical valve/anticoagulation

# Physical Activity Concerns in Marfan Syndrome and Related Disorders

aorta



The demands on the cardiovascular system differ among various types of exercise and physical activity.



## Dynamic (isotonic) exercise

- refers to shortening or lengthening of muscle fibers during contraction
- results in muscle movement
- blood vessels dilate
- modest increase in mean BP

# Physiologic response to exercise: Not all types of physical activity are the same



## Dynamic (isotonic) exercise

- refers to shortening or lengthening of muscle fibers during contraction
- results in muscle **movement**
- blood vessels dilate
- modest increase in mean BP



## Static (isometric) exercise

- refers to muscle contraction without movement
- vasoconstriction to non-contracting muscles
- ↑ flow to contracting muscles
- associated with increases in BP

## Competitive Athletics

- Systematic training
- Primary pursuit is athletic excellence and achievement
- Typically push to highest natural physical limits



## Recreational Athletics

- Non-competitive
- Light-to-moderate exercise
- Fitness and fun



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## Recreational Athletics

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Blood pressure and heart rate response to exercise depends upon the type of activity, the level of intensity, and the conditioning of the individual.

The **M**etabolic **E**quivalent of **T**ask (MET), or simply metabolic equivalent, is a physiological measure expressing the energy cost (or calories) of physical activities.

One MET is the energy equivalent expended by an individual while seated at rest.

While exercising, the MET equivalent is the energy expended compared to rest, so MET values indicate the intensity.

An activity with a MET value of 5 means you are expending 5 times the energy (number of calories) than you would at rest.

## Can One Predict BP Response to Various Levels of Physical Activity?

Systolic blood pressure may increase by 8 to 12 mm Hg per MET of aerobic activity with only minimal effect on diastolic BP.

Because higher blood pressure leads to greater aortic wall stress, it is recommended to limit activities which require extreme or maximal exertion, especially those requiring straining.

Light <3.0 METs	Moderate 3.0–6.0 METs	Vigorous >6.0 METs
<ul style="list-style-type: none"> <li>•Walking—slowly</li> <li>•Sitting—using computer</li> <li>•Standing—light work (cooking, washing dishes)</li> <li>•Fishing—sitting</li> <li>•Playing most musical instruments</li> </ul>	<ul style="list-style-type: none"> <li>•Walking—very brisk (4 mph)</li> <li>•Cleaning—heavy (washing windows, vacuuming, mopping)</li> <li>•Mowing lawn (power mower)</li> <li>•Bicycling—light effort (10–12 mph)</li> <li>•Badminton—recreational</li> <li>•Tennis—doubles</li> <li>•Leisurely swimming</li> <li>•Table tennis</li> <li>•Yoga</li> <li>•Pilates</li> <li>•Water aerobics</li> <li>•Golf (walking, pulling cart)</li> </ul>	<ul style="list-style-type: none"> <li>•Walking/hiking</li> <li>•Jogging at 6 mph</li> <li>•Shoveling</li> <li>•Carrying heavy loads</li> <li>•Bicycling fast (14–16 mph)</li> <li>•Basketball game</li> <li>•Soccer game</li> <li>•Tennis—singles</li> <li>•Heavy farming (baling hay)</li> </ul>

# Sports and Exercise

- The AHA/ACC Scientific Statement on Eligibility and Disqualification Recommendations for ***Competitive Athletes*** with Cardiovascular Abnormalities has divided sports into a classification scheme based upon **peak static** and **dynamic** components achieved during training and competition and **potential for bodily contact**

# Classification of Sports

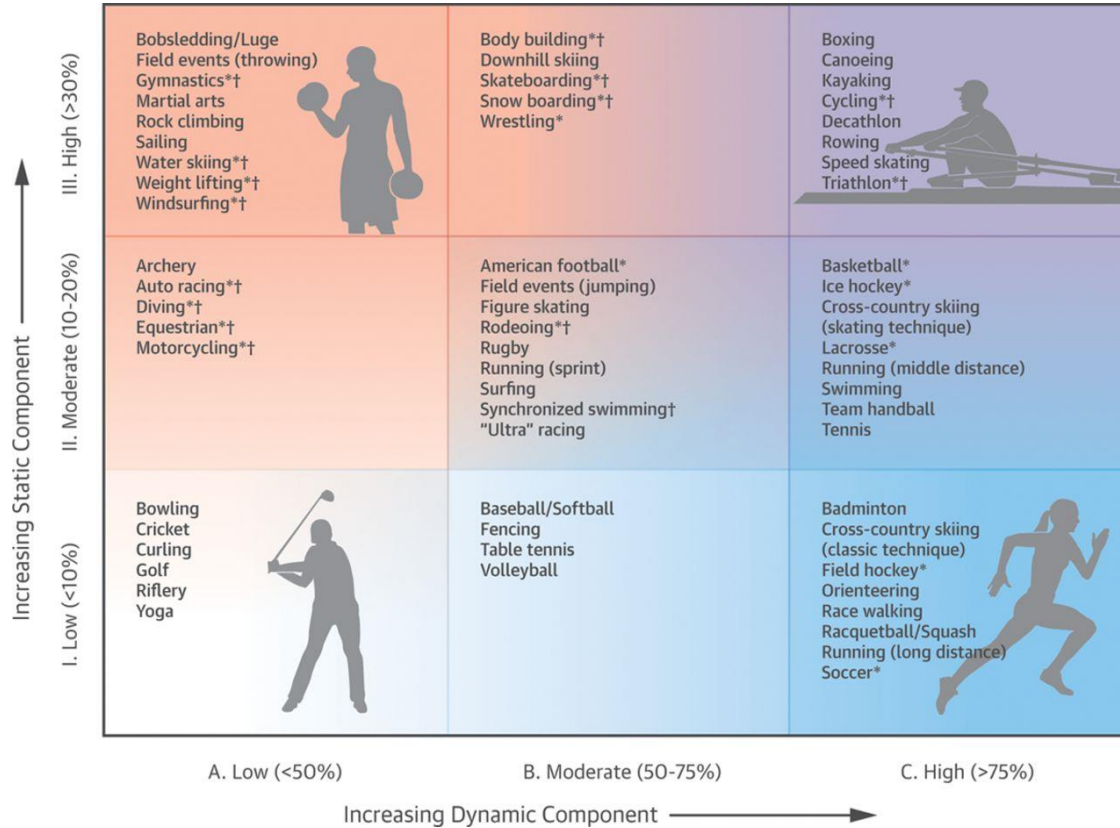
Levine AD, et al. JACC 2015;66:2350-3

Weight lifting,  
rock climbing...

Cycling,  
rowing

Golf,  
bowling,  
yoga...

Soccer, field  
hockey



# Competitive Sports according to impact and age/educational level

From: Levine et al. JACC 2015;66:230-3

	Junior High School	High School/College
Impact Expected	American football Ice hockey Lacrosse Wrestling Karate/Judo Fencing Boxing	American football Soccer Ice hockey Lacrosse Basketball Wrestling Karate/Judo Downhill skiing Squash Fencing Boxing
Impact May Occur	Soccer Basketball Downhill skiing Equestrian Squash Cycling	Field hockey Equestrian Cycling Baseball/softball Gymnastics Figure skating
Impact Not Expected	Baseball/softball Cricket Golf Riflery Gymnastics Volleyball Swimming Track and Field Tennis Figure skating Cross-country skiing Rowing Sailing Archery Weightlifting Badminton	Cricket Golf Riflery Volleyball Swimming Track and Field Tennis Cross-country skiing Rowing Sailing Archery Weightlifting Badminton

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From: Levine et al.  
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# Exercise and the Aorta

Does exercise cause aortic dissection?

Does exercise lead to progression dilatation (enlargement) of the aorta?

# Exercise and the Aorta

Studies of bodybuilders have demonstrated systolic BP  $>300$  mm Hg during maximal weightlifting.

Increase in BP occurs during Valsalva maneuver (bearing down).

Surges in BP can occur during intense isometric activity which may place significant transient stress on the aorta.



Kris Dim: bodybuilder

There are reports of acute aortic dissection related to intense physical activity such as weight lifting.

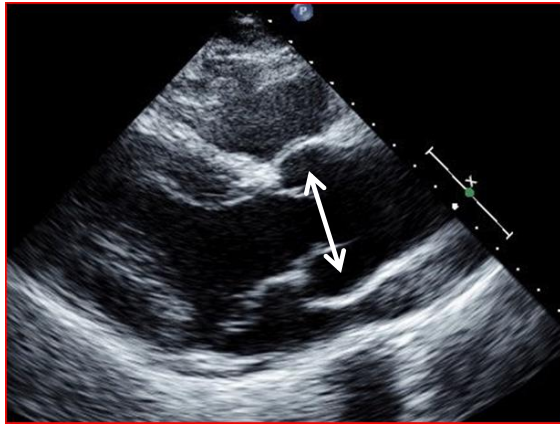
# Exercise and the Aorta

Does exercise cause aortic remodeling and enlargement?

# Exercise and the Aorta

Does exercise cause aortic remodeling and enlargement?

Aortic root size in >5000 elite athletes as compared to controls.



Mean aortic root size 3.2 mm larger in elite athletes

Aortic dimensions in endurance trained athletes tended to be larger than in strength-trained athletes.

Not controlled for BSA in many of the studies.

# Aortic Root Size in Elite Strength-Trained Athletes

Babaei Bigi et al. Am J Cardiol 2007;100:528-530

100 Male Professional strength-trained athletes (weight lifting, power lifting, body building) (mean age  $22.1 \pm 3.6$  years) referred to the Institute of Sports Science in Iran, 2001-2005.

Individuals with Marfan syndrome, Ehlers-Danlos syndrome and bicuspid aortic valve were excluded.

128 healthy age- and height-matched men were controls.

BP significantly higher in weight lifters 137/86 vs. 112/72

# Aortic Root Size in Elite Strength-Trained Athletes

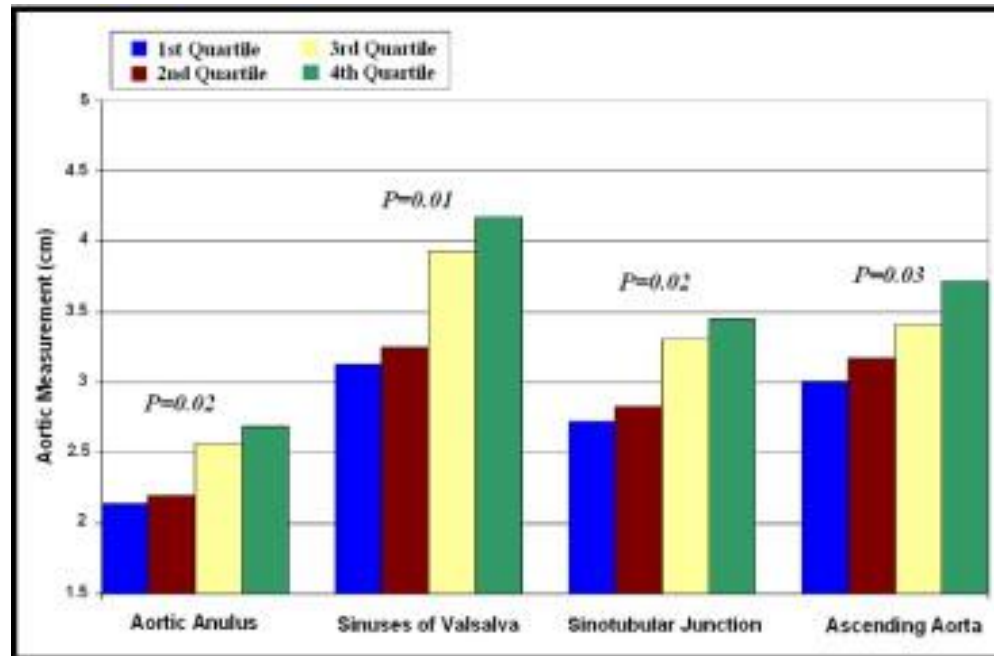
Babaee Bigi et al. Am J Cardiol 2007;100:528-530

	<b>Strength-Trained Athletes</b>		<b>Controls</b>		
	Mean	SD	Mean	SD	p-value
Sinus of Valsalva (cm)	3.82	0.41	3.16	0.32	<0.05
Sinotubular junction (cm)	3.41	0.28	2.95	0.31	<0.05
Ascending aorta (cm)	3.61	0.45	3.10	0.29	<0.05

Height, BP and duration of High Intensity Training all correlated with aortic root size.

# Aortic Root Size in Elite Strength-Trained Athletes

Babae Bigi et al. Am J Cardiol 2007;100:528-530



Aortic root size was largest in the elite strength-trained athletes who trained the longest.

(<18 months to >54 months)

# Sudden Death in Athletes is Uncommon

Maron BJ et al. Circulation 2007;115:1643-55.

## Incidence of Sudden Cardiac Death in Athletes

~1 in 200,000 young people of high school age per year

~1 in 123,000 male high school and college athletes per year

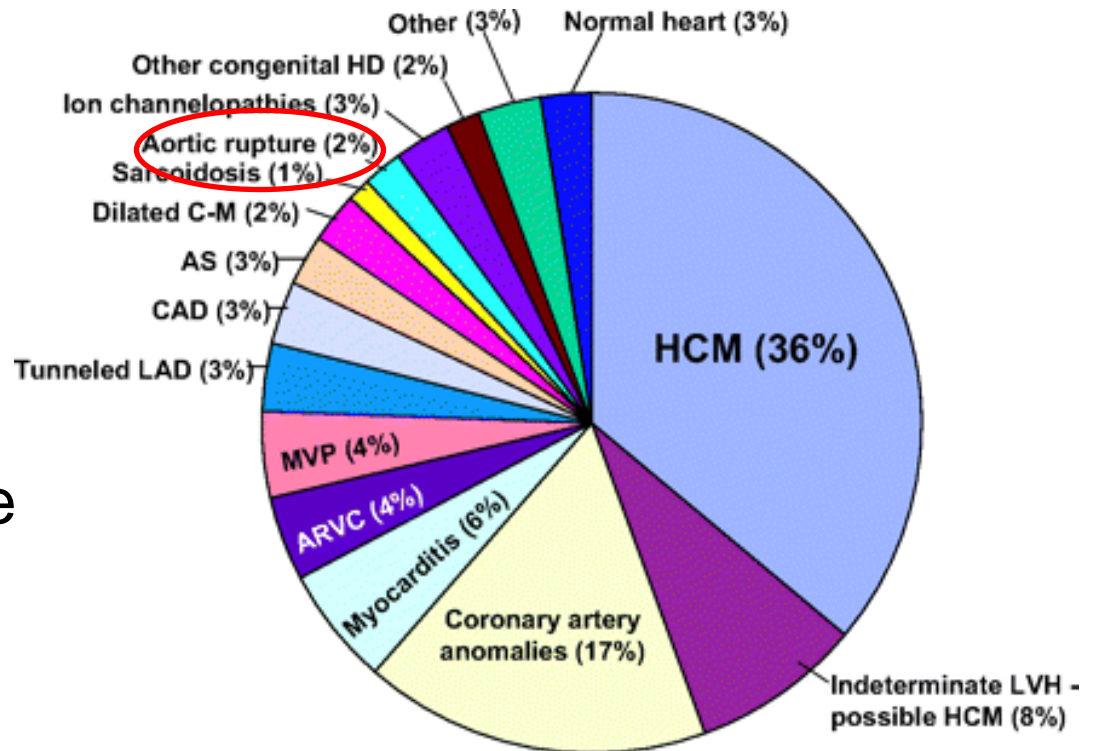
~1 in 769,000 female high school and college athletes per year

# Causes of Sudden Cardiac Death in Athletes

Maron BJ et al. Circulation 2007;115:1643-55.

800 sudden deaths related to sports in competitive athletes over a 27 year period.

- 19 (2%) aortic rupture



# What is known about the risk of aortic dissection during exercise in Marfan Syndrome?

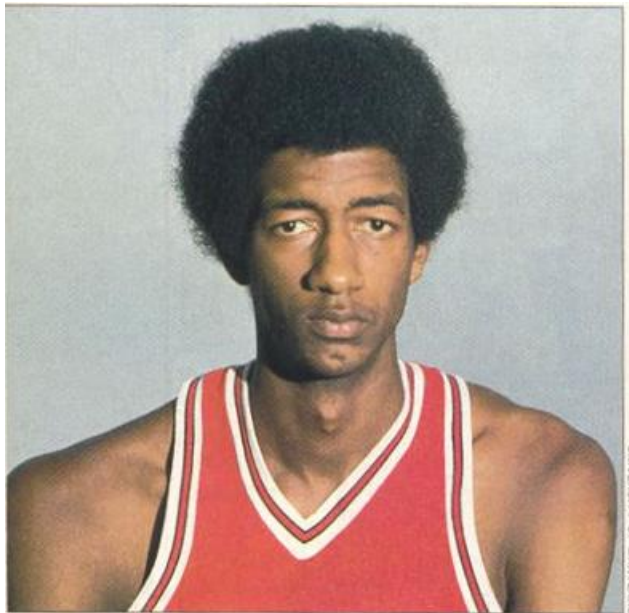
Very little data

Anecdotal information; high-profile cases...

# What is known about the risk of aortic dissection during exercise in Marfan Syndrome?

Very little data

Anecdotal information; high-profile cases..



Chris Patton 1976



Flo Hyman 1986

# Sudden Death due to Aortic Dissection or Rupture in Competitive Athletes

Harris KM et al. JACC 2015;65:860-62.

US National Registry of Sudden Death in Athletes

<40 years old

2588 deaths in registry

25 (1%) due to aortic dissection or rupture

Marfan syndrome either diagnosed (or suspected) in 12 cases

10:1 male to female

17.6  $\pm$  5 years old (range 11-36 years)

Basketball/football/baseball most common sports associated with SD.

2/3 of cases of aortic dissection occurred during physical exertion

What is known about the effect of intense exercise on the aorta in one with Marfan Syndrome?



Isaiah Austin 2014



Jonathan Jeanne 2017

The AHA/ACC has published Guidelines regarding a safe approach to **competitive** sports in people with Marfan syndrome and related disorders.

AHA/ACC SCIENTIFIC STATEMENT

Eligibility and Disqualification  
Recommendations for Competitive Athletes  
With Cardiovascular Abnormalities:  
Task Force 7: Aortic Diseases,  
Including Marfan Syndrome

A Scientific Statement From the American Heart Association and American College of Cardiology  
Journal of the American College of Cardiology 2015;66:2398-2405

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Society	Recommendations
COMPETITIVE ATHLETES ACC/AHA Guidelines* (2015)	It is reasonable for athletes with Marfan syndrome to participate in <b>low and moderate static/low dynamic competitive sports (classes IA and IIA)</b> if they do not have $\geq 1$ of the following :  a. Aortic root dilatation b. Moderate to severe mitral regurgitation c. Left ventricular systolic dysfunction (ejection fraction $< 40\%$ ) d. Family history of aortic dissection at an aortic diameter $< 50$ mm

**IA:** Golf, billiards, bowling, cricket, curling, riflery

**IIA:** Archery

\*Braverman AC et al. J Am Coll Cardiol 2015;66:2398-2405

Society	Recommendations
COMPETITIVE ATHLETES	
ACC/AHA Guidelines* (2015)	<p>It is reasonable for athletes with Loeys-Dietz syndrome, FTAA syndrome or vascular Ehlers-Danlos syndrome to participate in <b>low static, low dynamic sports (class IA)</b> if they do not have any of the following:</p> <ul style="list-style-type: none"> <li>a. Aortic enlargement or dissection, or branch vessel enlargement</li> <li>b. Moderate to severe mitral regurgitation</li> <li>c. Extracardiac organ system involvement that makes participation hazardous</li> </ul>

**IA:** Golf, billiards, bowling, cricket, curling, riflery

\*Braverman AC et al. J Am Coll Cardiol 2015;66:2398-2405

Society	Recommendations
COMPETITIVE ATHLETES  ACC/AHA Guidelines* (2015)	Athletes with Marfan syndrome, familial TAA syndrome, Loeys-Dietz syndrome, unexplained aortic aneurysm, vascular Ehlers-Danlos syndrome, or a related aortic aneurysm disorder <u>should not participate in any competitive sports</u> that involve <b>intense physical exertion</b> or the potential for <b>bodily collision</b>

\*Braverman AC et al. J Am Coll Cardiol 2015;66:2398-2405

## Medications, Physical Activity and Sports

**Beta-blockers:** reduce heart rate and lessen the force generated by the heart during contraction

- Will limit heart rate response during physical activities
- Do not allow the person with Marfan syndrome or a related disorder to perform strenuous exercise or contact sports

**Losartan:** does not have any effect on heart rate at rest or with exertion

**Warfarin (Coumadin):** anticoagulant which increases risk of bleeding related to trauma, falls, etc.

- Avoid contact sports, activities at risk for bleeding during fall (skiing, etc.)

# Mild aerobic exercise protects aortic structure and function in a mouse model of Marfan syndrome.

Gibson C, et al. J Appl Physiol 2017 doi:10.1152/jappphysiol.00132.2017

4-week old Marfan and wild-type mice were subjected to voluntary and forced exercise regimens, or a sedentary lifestyle for 5 months.



# Mild aerobic exercise protects aortic structure and function in a mouse model of Marfan syndrome.

Gibson C, et al. J Appl Physiol 2017 doi:10.1152/jappphysiol.00132.2017

Marfan mice that exercised had improved aortic wall structure and function, with beneficial effect optimum at low intensity exercise (~60% of  $\dot{V}O_2$  max) and tapering off at higher intensity of exercise (85% of  $\dot{V}O_2$  max).

Enzymes which lead to the breakdown of matrix proteins (MMP-2 and MMP-9) demonstrated less expression within the aortic wall of Marfan mice that exercised.

# Survivors of Aortic Dissection: Activity, Mental Health, and Sexual Function

Chaddah A, Klein-Rodgers E, Braverman AC, et al.  
Clin Cardiol 2015;38:652-9.

314 survivors of acute aortic dissection surveyed regarding lifestyle modifications, exercise practice and emotional state. Response rate was 42%.

32% with new-onset depression

32% with new onset anxiety

24% no longer engaged in any exercise

Majority of patients no longer sexually active after aortic dissection

Those who exercised routinely had less depression and lower BP.

## Approaching Exercise and Physical Activity in a Safe and Practical Manner

What advice is recommended regarding ***recreational (non-competitive)*** exercise and physical activity in individuals with Marfan syndrome and related disorders?

# Guidelines for Recreational (Non-Competitive) Sports and Exercise

Society/Organization	Recommendations for those with Marfan syndrome and Related Disorders
<b>Recreational (Non-Competitive) Exercise</b>	
ACC/AHA, ESC	<ul style="list-style-type: none"><li>• Avoid collision sports and strenuous activities involving lifting, pushing or straining that require Valsalva</li><li>• Avoid intense isometric activities</li></ul>
Marfan Foundation	<ul style="list-style-type: none"><li>• Favor non-competitive, dynamic exercises such as walking, jogging, leisurely bicycling or slow-paced tennis</li><li>• Avoid isometric activities (push-ups, sit-ups, weightlifting)</li><li>• Avoid intense contact sports</li></ul>
Loeys-Dietz Foundation	<ul style="list-style-type: none"><li>• Remain active with aerobic activities performed in moderation (hiking, biking, jogging, swimming)</li><li>• Avoid competitive sports, esp. contact sports, or muscle straining activities performed to the level of exhaustion</li><li>• Avoid straining activities (push-ups, chin-ups, sit-ups)</li></ul>

## Recreational (non-competitive) Sports and Exercise Recommendations in Marfan syndrome and Related disorders (in the absence of significant aortic dilatation)

Permitted	Intermediate*	Strongly Discouraged
Bowling Golf Brisk walking Modest hiking Doubles tennis Treadmill Stationery bike Archery Table tennis Light weightlifting with repetitions Yoga, Pilates	Singles tennis Baseball/Softball Hiking Swimming (lap) Horseback riding Biking Ice skating Racquetball Dancing Jogging Badminton	Body building Ice hockey Rock climbing Windsurfing Surfing Scuba Diving Weightlifting Football

\*intermediate activities should be assessed clinically with recommendations based on individual circumstances

# Recommendations for Physical Activity and Exercise in Marfan Syndrome and Related Disorders

Stay at an aerobic level of exercise wherein one can talk in a conversational voice during the activity, or using a perceived activity scale:

RPE Scale	Rate of Perceived Exertion
10	<b>Max Effort Activity</b> Feels almost impossible to keep going. Completely out of breath, unable to talk. Cannot maintain for more than a very short time.
9	<b>Very Hard Activity</b> Very difficult to maintain exercise intensity. Can barely breath and speak only a few words
7-8	<b>Vigorous Activity</b> Borderline uncomfortable. Short of breath, can speak a sentence.
4-6	<b>Moderate Activity</b> Breathing heavily, can hold short conversation. Still somewhat comfortable, but becoming noticeably more challenging.
2-3	<b>Light Activity</b> Feels like you can maintain for hours. Easy to breathe and carry a conversation
1	<b>Very Light Activity</b> Hardly any exertion, but more than sleeping, watching TV, etc

Physical activity is important for one's health and well-being.



No matter how slow you go, you are still lapping everybody on the couch.



THE **MARFAN**  
FOUNDATION

Know the signs. Fight for victory.

Thank You and “Protect the Tube of Life!”

